UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/719,533	07/10/2001	Chong Jin Oon	U 013108-9	8503

140 7590 08/10/2004

LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 08/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,533	OON ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *15-24 and 27-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,10-14,25 and 26* is/are rejected.

7)☐ Claim(s) *3, 9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12-13-00*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently claims 1-74 are pending in the application. In the prior action, mailed on December 16, 2003, claims 2-12, and 14 were rejected, and claims 1, 13, and 15-74 were withdrawn as to non-elected inventions. The Applicant's arguments in traversal are noted. However, they are not found persuasive as the nucleotide of claim 2 is not considered to share a common special technical feature that distinguishes over the prior art. See e.g., the Ho reference sited below. Thus, the restriction is maintained.

2. The restriction between claims 2-12, and 14, and previously withdrawn claims 1, 13, 25, and 26 is withdrawn.

3. Claims 1-14, 25, and 26 are pending and under consideration.

4. The examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

5. Because this action raises new grounds of rejection, the action is made Non-final.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on December 13, 2000, complies with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

7. **(New Objection)** The disclosure is objected to because of the following informalities: the application indicates that the polypeptide of SEQ ID NO: 3 is encoded by the nucleic acid of SEQ ID NO: 1. See, page 6, description of Figure 5 (indicating that SEQ ID NO: 3 is the amino acid of the S protein encoded by SEQ ID NO: 1). However, a comparison of SEQ ID NO: 1 (and in particular bases 287-292 of the sequence) with SEQ ID NO: 3 (esp. residues 219 and 220) shows that the amino residues 219 and 220 placed in the order proline-threonine should, according to the coding sequence of SEQ ID NO: 1, read threonine-proline.

Appropriate correction is required.

It is noted that amendments to the sequences should also be reflected in both the paper copy and the computer readable form of the sequence listing.

8. **(New Objection)** The specification is objected to because the description of the Figures provided on pages 6-8 of the application indicate that there are 13 Figures in the Application. However, only pages of drawings are present in the application; a first apparently corresponding to described Figure 1, and a second that does not appear to correspond to any of the described figures. It is suggested that the Applicant either amend the application such that the description of the figures corresponds to the figures present in the application.

Applicant is cautioned against the amendment of the specification such that New Matter is introduced into the disclosure.

9. **(New Objection)** The disclosure is objected to because of the following informalities: in several instances (pages 4, 11, 18, 25, and 32) the text of the specification is faded such that it is not legible.

Appropriate correction is required.

Claim Objections

10. **(Prior Objection- Maintained)** Claim 4 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. This claim purports to further limit the invention of claim 3 to embodiments wherein the isolated nucleic acid of SEQ ID NO: 3 comprises the sequence AGA at positions 587-89. The Applicant traverses the objection on the basis that "although claim 3 requires that the recited polypeptide comprise nucleotides 155 through 835 of SEQ ID NO: 1, it does not require that the nucleotides be in designated positions within the polypeptide. Thus, the recited polypeptide can also contain other nucleotides and need not have "AGA" at positions 587-589." It is not entirely clear what the Applicant is attempting to argue. However, it appears that the Applicant is asserting that the nucleic acid of SEQ ID NO: 1 may comprise other sequences that "AGA" at positions 587-589. This argument is not found persuasive.

If claim 4 were dependant on claim 2, which relates to a nucleic acid encoding the indicated polypeptide generally, the Applicant's argument would have merit. However, in the instant case, claim 4 is dependant on claim 3, which requires that the claimed nucleic acid have the specific sequence disclosed in SEQ ID NO: 1. As per the sequence listing, positions 587-589 of this sequence have the sequence AGA. The "further limitation" of claim 4 is in fact an

inherent property of SEQ ID NO: 1. Thus, claim 4 may be further limiting to claims which read on generic nucleic acid sequences encoding the polypeptide of claim 2, and wherein such nucleic acids comprise sequences wherein the nucleic acids corresponding to residues 587-589 have the sequence AGA. Such is not the case, however, where the claim from which claim 4 depends requires a specific nucleic acid sequence. The objection is therefore maintained.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. **(New Rejection)** Claims 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on oligonucleotides that hybridize to "a unique sequence of nucleotides within a nucleic acid which encodes a polypeptide which is a major surface antigen of a strain of hepatitis B virus... without hybridizing to any sequence of nucleotides within a nucleic acid which encodes the major surface antigen of a wild type hepatitis B virus." Claim 26 further limits the oligonucleotides to that that comprise nucleotides 527-595 of SEQ ID NO: 1. These claims are indefinite for three reasons.

First, it is unclear what is meant by a "unique sequence of nucleotides."

Second, it is unclear how an oligonucleotide comprising residues 527-595 of SEQ ID NO: 1 can hybridize to a nucleotide encoding the major surface antigen of a hepatitis B virus

where SEQ ID NO: 1 itself is disclosed as a nucleotide that encodes the antigen. I.e., it is unclear how a nucleotide can hybridize to itself, or a mutagen of itself.

Third, it is unclear how an oligonucleotide can hybridize to a nucleic acid encoding a mutant of the major surface antigen of a hepatitis B virus without also being capable of hybridizing to a nucleic acid that encodes a wild-type sequence of the protein. Because a nucleotide that encodes a mutant of the HBV protein would inherently include nucleic acid sequences that encode polypeptides of a wild type viral protein, it is not clear how an oligonucleotide could by hybridize to the mutant, and not to the wild-type sequence.

Clarification is required.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. **(New Rejection)** Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim is rejected because the claim depends for enablement on a **Deposit without a promise for availability.** The viruses deposited as accession numbers P97121504, P97121505, and P97121506 are required to practice the claimed invention. This is because the claimed invention is the deposited isolated viruses. As a required element, it must be known and readily available to

the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the claimed/described viruses. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the viruses and it is not apparent if it is readily available to the public. Applicant's deposit statement on specification page 4 does not indicate the extent of public availability. If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. **(Prior Rejection- Withdrawn)** Claims 2, 5-9, 12, and 14 were rejected under 35 U.S.C. 102(b) as being anticipated by WO 91/14703. The claims have been amended such that

they now require that the encoded polypeptide is a mutant major surface antigen of a subtype *adw* Hepatitis B virus. In view of the amendment of the claims, the rejection is withdrawn.

17. **(Prior Rejection- Withdrawn)** Claims 2-5 and 8-11 were rejected under 35 U.S.C. 102(b) as being anticipated by Oon et al. (Vaccine 13(8): 699-702). The claims have been amended as described above. In view of the arguments presented by the applicant in traversal of the rejection (regarding the failure of the reference to teach the molecular structure of the

18. **(New Rejection)** Claims 2, 5, 8, 10, 11, 25, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Ho et al. (Clin Diagn Lab Immunol 2(6): 760-62). The claims have been described above, or in the prior action. For the purposes of this rejection, claims 25 and 26 are read as describing oligonucleotides that would hybridize to either SEQ ID NO: 1 or its complement. Ho discloses on page 760 the sequence of the genome fragment encoding the a determinant of a mutant HBV virus wherein residue 145 of the S protein has been mutated from a glycine to an arginine. The sequence of the sequenced viral PCR nucleotide and the encoded protein are provided in Figure 1. The disclosed amino acid sequence is identical positions 298-320 of SEQ ID NO: 3 in the present application. Further, because the reference teaches that the sequences nucleotides were amplified through PCR, the reference inherently teaches the use of oligonucleotides that can hybridize to SEQ ID NO: 1 (i.e. primers for the PCR amplification). The reference therefore anticipates the indicated claims.

It is noted that the reference does not specify that the disclosed sequence is from a subtype adw HBV. However, because the sequence disclosed in the reference is identical to that

required in the claims, the disclosed sequences meet the structural requirements of the claims. Because the sequence meets the structural requirements of the claims, the source of the fragment is not sufficient to distinguish the claimed sequences from that of the structurally identical prior art.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. **(Prior Rejection- Withdrawn)** Claims 6, 7, 12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oon in view of WO 91/14703. The rejection is withdrawn for the reasons indicated above with respect to the 102 rejections over each of Oon and the WO 91/14703 reference.

21. **(New Rejection)** Claims 2, 5, 8, 10-14, 25, and 26 rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al. (supra) in view of WO 91/14703. These claims read on the nucleic acids described above, and vectors comprising them. The teachings of Ho have been described in part above. The reference teaches that the 145-arginine HBV variant is an escape mutant not affected by normal anti-HBV vaccination, and suggests that anti-HBV vaccines require improvement to circumvent the presence of escape mutant viruses. The reference does not however suggest the making of vectors encoding the mutant protein. However, the WO

91/14703 document, which provides similar teachings with reference to a 145-arginine mutant of a HBV subtype ayr sequence, teaches the production of vectors encoding the sequence, and vectors encoding the "a determinant" of the protein. Claim 1. In view of these combined teachings suggesting the making of vaccines against 145-arginine HBV variants, it would have been obvious to those in the art to isolate nucleic acids encoding the mutant protein comprising residues 298-320 of SEQ ID NO: 3, and to make vectors comprising such nucleic acids. The combined teachings of these references therefore render the claims obvious.

22. **(New Rejection)** Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho in view of WO 91/14703 as applied above, and further in view of U.S. Patent 5,830,759. The indicated claims further identify the claimed nucleic acids as DNA, RNA, cDNA, or genomic nucleic acids. Neither of Ho nor WO 91/14703 teach isolated nucleic acids other than DNA. However, as is clear from the teachings of the 5,830,759 (see e.g., claims 1-4), the making and use of any of the indicated types of nucleic acids are known in the art. It would therefore have been obvious to those in the art to make nucleic acids comprising any of these types of nucleic acids.

Conclusion

23. No claims are allowed. Claims 3 and 9 are objected for depending on rejected claims.

24. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Each of Norder et al., J Gen Virol 73: 1201-08, and Norder et al., J Gen Virol 74:1341-48 are considered relevant in that they each teach at least one of an amino acid sequence, or a DNA sequence encoding, the HBV surface antigen of a subtype adw Hepatitis B virus. However, it is also noted that none of the disclosed sequences exactly matches those disclosed in SEQ ID NOs: 1 and 3 of the present application.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 8/7/04
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600